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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
BAUM, STUART F

ART UNIT	PAPER NUMBER
1638	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/824,735	ZHU ET AL.	
	Examiner	Art Unit	
	Stuart F. Baum	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *23-31 and 36-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22 and 32-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-42 are pending.

2. Applicant's election with traverse of Group I, claims 1-22 and 32-35 including SEQ ID NO:1 encoding SEQ ID NO:2, in Paper No. 9 is acknowledged. The traversal is on the ground(s) that the Office has not provided sufficient reasons and/or examples to support the assertion that the groups are unrelated. In addition, Applicants assert that a search of all claims would not constitute a serious burden on the Office especially because Groups I and VI and Groups II and III are classified in the same subclasses.

This is not found persuasive because as stated in the restriction requirement, the method steps of Groups I-VII are distinct which is sufficient reason to support the assertion that the groups are unrelated. Groups can be classified in the same subclass and still be distinct because while the search of the prior art for one group may overlap with that of another, they are not co-extensive of each other and thus would be a burden on the Office.

The requirement is still deemed proper and is therefore made FINAL.

Claims 23-31 and 36-42 are withdrawn from consideration because they are drawn to a non-elected invention.

Claims 1-22 and 32-35 are examined on their merits.

Specification

3. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01 (see for example page 12, lines 21-22).

On page 6, line 20, "solution" is misspelled.

On page 1, line 24, "growth" is misspelled.

On page 1 line 22, "Sensitive2" is misspelled.

Drawings

4. The drawings are objected to for the reasons indicated on the enclosed form PTO-948. Correction is required. Figure 4 is missing the picture of the coomassie stained gel and exposed x-ray film.

Information Disclosure Statement

5. The information disclosure statement filed 8/17/2001 fails to comply with 37 CFR 1.98(a)(1), which requires a list of all patents, publications, or other information submitted for consideration by the Office. It has been placed in the application file, but the information referred to therein has not been considered.

Claim Objections

6. Claim 33 is objected to for being a duplicate claim of claim 32.

Claim 35 is objected to for being a duplicate claim of claim 34.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 4-8, 34 and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 does not further limit claim 3, as the claim does not specify a "fully complimentary sequence". As written, the claim reads on a sequence that is complimentary to a single base pair of SEQ ID NO:1.

Claims 5-8 do not further limit the claim from which they are dependent. As written, the claims encompass a greater number of sequences than claim 3. Amending the claims to be independent claims will obviate the rejection.

In claims 34 and 35, "increasing" is a relative term and lacks a comparative basis.

In claims 34 and 35 "in need thereof" is superfluous and it is suggested to delete this phrase.

Claims 34 and 35 are missing methods steps. The claims should be amended to recite that the polynucleotide of claim 1 is expressed at a particular level which confers salt tolerance to said plant. Clarification and/or correction are required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 1-22 and 32-35 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible asserted utility or a well established utility.

The claims are drawn to an isolated polynucleotide which encodes a polypeptide of SEQ ID NO:2, an isolated polynucleotide of SEQ ID NO:1, or a polynucleotide sequence which is at least 70%, 80%, or 90% identical to the polynucleotide of SEQ ID NO:1, or a purified polynucleotide that hybridizes under particular stringency conditions to SEQ ID NO:1; vectors, host cell, plant cell, and transgenic plant comprising an above mentioned sequence. Applicant also claims method of making a transgenic plant and method of increasing the salt tolerance of a plant, both methods comprise transforming the plant with a polynuceotide that encodes a polypeptide of SEQ ID NO:2.

Applicants' invention is SEQ ID NO:1 (*SOS2*) encoding a serine/threonine protein kinase. Mutations in *SOS2* cause Na^+ and K^+ imbalance and render plants more sensitive towards growth inhibition by high Na^+ and low K^+ environments (page 1, lines 23-24). *SOS2* was positionally cloned from *Arabidopsis* and is expressed constitutively through out the plant but is upregulated in the roots in response to NaCl treatment. Phosphorylation by *SOS2* depends on the presence of both *SOS3* and Calcium (page 16, lines 8-9).

Applicants have disclosed that their invention is a protein kinase and that there are many substrates that will be phosphorylated by the *SOS2* protein kinase (page 16, lines 7-8). However, based upon Applicant's disclosure, there is no clear nexus between their invention of SEQ ID

NO:1 and any utility set forth to allow one skilled in the art at the time the invention was made to take the claimed invention and clearly and immediately achieve the benefits set forth. There are many protein kinases, and they are all structurally and fuctionally distinct from each other. Each is involved in different processes resulting from different pathways. Without knowing which pathway of which process Applicant's SEQ ID NO:1 is involved in, and how SEQ ID NO:1 can be used to achieve a particular result, it is unclear how one skilled in the art would use the claimed invention.

In regards to Applicant's SEQ ID NO:1, how and under what conditions should a nucleic acid encoding a serine/threonine kinase of SEQ ID NO:1 be used to enhance salt tolerance. In which tissues does it need to be expressed to achieve the purported advantage. Given that *SOS2* requires the presence of *SOS3*, will the purported increase in salt tolerance be achieved if there is not a concomitant increase in *SOS3* activity? It is apparent that extensive further research, not considered to be routine experimentation, would be required before one skilled in the art would know how to use the claimed invention. It has been established in the courts that a utility which requires or constitutes carrying out further research to identify or reasonably confirm a "real world" context of use is not a substantial utility:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an application to engross what may prove to be a broad field." (*Brenner v. Manson,* 383 U.S. 519 (1966)).

Thus, while a developmental process such as salt tolerance would provide substantial benefit to the public, it is unclear how one of ordinary skill in the art would be able to utilize Applicant's nucleic acid of SEQ ID NO:1 encoding a serine/threonine protein kinase to increase

salt tolerance without having to carry out further research. Accordingly, the claimed invention lacks a "real-world" use.

In addressing claims drawn to sequences having 70%, 80%, or 90% sequence identity to the polynucleotide of SEQ ID NO:1, or a purified polynucleotide that hybridizes under particular stringency conditions to SEQ ID NO:1, since SEQ ID NO:1 lacks utility for the reasons set forth above, sequences having less than 100% sequence identity to SEQ ID NO:1 would also lack utility. Again, Applicant should note that no region of the protein encoded by SEQ ID NO:1 has been identified to be essential for its proper acitivy. Also, no working examples of any such sequence having 70%, 80%, or 90% sequence identity to the polynucleotide of SEQ ID NO:1, or a purified polynucleotide that hybridizes to SEQ ID NO:1, are set forth in Applicant's disclosure.

Additionally, there also is no well-established utility for SEQ ID NO:1. SEQ ID NO:1 does not have a well-established utility for hybridization purposes because the encoded protein does not have utility for the reasons indicated above. Accordingly, the claimed invention lack utility.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-22 and 32-35 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Written Description

10. Claims 5-8, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated polynucleotide which is at least 70%, 80%, or 90% identical to the polynucleotide of SEQ ID NO:1, or a purified polynucleotide that hybridizes under particular stringency conditions to SEQ ID NO:1; vectors, host cell, plant cell, and transgenic plant comprising an above mentioned sequence. The specification only discloses the nucleic acid sequence of SEQ ID NO:1 encoding a *Salt Overly Sensitive 2* (*SOS2*) serine/threonine protein kinase polypeptide and does not disclose any specific structural, physical and/or chemical properties for the claimed sequence. Applicant does not present a description of domains that are specific to this particular serine/threonine protein kinase nor domains that are important for its proper function. Applicant's stringent conditions would allow for hybridization to sequences which may not have known serine/threonine kinase activity, which Applicants are clearly not in possession of. Given the lack of description, one skilled in the art would not be able to identify sequences with less than 100% sequence identity that still maintained the proper activity. Therefore, the written description requirement is not satisfied. Therefore, one skilled in the art would not recognize from the disclosure that Applicant was in possession of the claimed invention. (see Written Description Requirement published in Federal Register/Vol.66, No. 4/ Friday, January 5, 2001/Notices; p. 1099-1111).

Enablement

11. Claims 1-22 and 32-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claimed invention is not supported by an enabling disclosure taking into account the *In re Wands* factors (858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are drawn to an isolated polynucleotide which encodes a polypeptide of SEQ ID NO:2, an isolated polynucleotide of SEQ ID NO:1, or a polynucleotide sequence which is at least 70%, 80%, or 90% identical to the polynucleotide of SEQ ID NO:1, or a purified polynucleotide that hybridizes under conditions which Applicant recites as stringent conditions to SEQ ID NO:1 but which are not stringent as interpreted by one skilled in the art; vectors, host cell, plant cell, and transgenic plant comprising an above mentioned sequence. Applicant also claims method of making a transgenic plant and method of increasing the salt tolerance of a plant, both methods comprise transforming the plant with a polynuceotide that encodes a polypeptide of SEQ ID NO:2.

Applicants' invention is SEQ ID NO:1 (*SOS2*) encoding a serine/threonine protein kinase. Mutations in *SOS2* cause Na^+ and K^+ imbalance and render plants more sensitive towards growth inhibition by high Na^+ and low K^+ environments (page 1, lines 23-24). *SOS2* was positionally cloned from *Arabidopsis* and is expressed constitutively through out the plant but is upregulated in the roots in response to NaCl treatment. Phosphorylation by *SOS2* depends on the presence of both *SOS3* and Calcium (page 16, lines 8-9).

Applicants have not taught how one skilled in the art would make a plant with increased salt tolerance using SEQ ID NO:1. Applicants teach that *Arabidopsis* plants comprising a mutant *sos2* gene are less tolerant of high Na^+ environments or Na^+ / K^+ imbalances but Applicants have not taught that plants transformed with SEQ ID NO:1 or sequences that exhibit 70%, 80%, or 90% identity to SEQ ID NO:1, or sequences that hybridize to SEQ ID NO:1 will have increased salt tolerance.

Halfter et al (2000, PNAS 97(7):3735-3740) teach that *SOS3* physically interacts with and activates *SOS2* protein kinase (abstract). Halfter et al also teach that results from a mutational analysis suggest that the two *SOS* genes are part of the same signal transduction pathway as the double mutant does not produce an additive effect when the two mutations are combined (page 3735, left column, last sentence). In addition, there exists other protein kinases that interact with *SOS3* that exhibit approximately 70% sequence identity with SEQ ID NO:2 (Figure 2, page 3738). Given that *SOS2* interacts with *SOS3*, and given that there are other putative kinases that interact with *SOS3*, it is not clear if over-expressing *SOS2* will increase the salt tolerance of a plant without also increasing the activity of *SOS3*. In addition, Larkin et al (1994, The Plant Cell 6:1065-1076) teach the unpredictability of transforming a plant to produce

the opposite phenotype as the mutant-gene phenotype. Larkin et al teach that *GLABROUS1* (*GL1*) mutant plants have a reduced number of trichomes. Over-expressing GL1 in *Arabidopsis* does not produce plants with an increased number of trichomes compared to wild-type plants (page 1072, right column, 1st paragraph). Therefore, just because the *sos2* mutants exhibit an increased sensitivity to high Na^+ concentrations, does not mean that over-expressing *SOS2* will automatically produce plants with an increased tolerance to Na^+.

It cannot be predicted by one of skill in the art that nucleic acids exhibiting 70% to 90% sequence identity to SEQ ID NO:1 and sequences that hybridize to SEQ ID NO:1 will encode a protein with the same activity as the polypeptide encoded by SEQ ID NO:1. Bowie et al (1990, Science 247:1306-10) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of the protein to fold into unique three-dimensional structures that allows it to function and carry out the instructions of the genome. The cited reference also teaches that the prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex (pg 1306, left column). Bowie et al teach that while it is known that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or none at all (pg 1306, right column). The sensitivity of proteins to alterations in even a single amino acid in a sequence is exemplified by McConnell et al (2001, Nature 411 (6838):709-713), who teach that the replacement of a glycine residue located within the START

domain of either the PHABULOSA or PHAVOLUTA protein receptor with either an alanine or aspartic acid residue, alters the sterol/lipid binding domain. This change renders the protein constitutively active and therefore creates a dominant mutation which has a drastic alteration in phenotype compared to wild-type *Arabidopsis* plants. For the *SOS2* encoding polynucleotide of SEQ ID NO:1, Liu et al (2000 PNAS 97(7):3730-3734) present an example of a *SOS2* allele in which one base change renders the protein kinase inactive (page 3734, left column, 3rd paragraph).

The claims are broadly drawn to nucleic acid sequences that hybridize to SEQ ID NO:1 but Applicant has not provided guidance for selecting sequences that encode a protein whose function is the same as the protein encoded by SEQ ID NO:1. The state of the art teaches isolating DNA fragments using stringent hybridization conditions, does not always select for DNA fragments whose contiguous nucleotide sequence is the same or nearly the same as the probe. Fourgoux-Nicol et al (1999, Plant Molecular Biology 40 :857-872) teach the isolation of a 674bp fragment using a 497bp probe incorporating stringent hybridization conditions comprising three consecutive 30 minute rinses in 2X, 1X and 0.1X SSC with 0.1% SDS at 65^{0}C (page 859, left column, 2nd paragraph). Fourgoux-Nicol et al also teach that the probe and isolated DNA fragment exhibited a number of sequence differences comprising a 99bp insertion within the probe and a single nucleotide gap, while the DNA fragment contained 2 single nucleotide gaps and together the fragments contained 27 nucleotide mismatches. Taking into account the insertions, gaps and mismatches, the longest stretch of contiguous nucleotides to which the probe could hybridize consisted of 93bp of DNA (page 862, Figure 2). In the present example, the isolated fragment exhibits less than 50% sequence identity with the probe. In the

present application, the selected sequences will encode proteins having modifications including additions, deletions, and substitutions of many amino acids when compared to a protein encoded by SEQ ID NO:1. Applicant's stringent condition is low and would allow for hybridization to sequences having no known serine/threonine kinase activity. Therefore, it is unpredictable as to whether any of the encoded proteins will have the same function as the protein encoded by SEQ ID NO:1.

Therefore, given the lack of guidance and examples of how one would make a plant with increased salt tolerance; given the breath of the claims that encompass exemplified and non-exemplified sequences; given the lack of guidance and examples; given the unpredictability; and the state of the art as discussed above, undue experimentation would be required by one skilled in the art to isolate a sequence encoding a protein with the same activity as the protein encoded by SEQ ID NO:1 and to use said sequence to make a plant with increased salt tolerance.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 4 is rejected under 35 U.S.C. 102(b) as being anticipated by Boudet et al (September, 1995 U.S. Patent Number 5,451,514.

The claim is drawn to a sequence which is complimentary to SEQ ID NO:1. The office interprets claim 4 to read on any sequence because Applicants have not specified a sequence that

is "fully" complimentary to SEQ ID NO:1. As written, a compliment sequence can comprise one base pair.

Boudet et al teach a DNA sequence that shares at least one base pair with SEQ ID NO:1 and as such, Boudet et al anticipate the claimed invention.

12. No claims are allowed. SEQ ID NO:1 and 2 are free of the prior art.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart Baum whose telephone number is (703) 305-6997. The examiner can normally be reached on Monday-Friday 8:30AM – 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 or (703) 305-3014 for regular communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the legal analyst, Gwendolyn Payne, whose telephone number is (703) 305-2475.

Phuong Bui

PHUONG T. BUI
PRIMARY EXAMINER

11/18/02

Stuart Baum Ph.D.

November 18, 2002